Eptinezumab reduced disease burden in chronic migraine and medication-overuse headache in patients also receiving patient education: Results from the placebo-controlled RESOLUTION trial

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These data from secondary outcomes show a greater impact of eptinezumab treatment vs placebo across several patient-reported outcomes measuring disease burden and health-related quality of life in adults with chronic migraine and medication-overuse headache who also received a brief educational intervention prior to dosing.

Background

- Medication-overuse headache (MOH) is a highly disabling and prevalent disorder occurring in ~60 million people worldwide, of which many are diagnosed with chronic migraine (CM), and can contribute to several negative outcomes for an individual.[1-4]
- MOH is diagnosed when a person with an existing headache disorder develops a new or worsened headache in association with medication overuse.[5]
- Currently, European guidelines recommend education about MOH as the primary treatment approach,[6] but multiple clinical approaches are used to treat MOH—patient education, preventive treatment alone, withdrawal from the overused medication alone, and combined medication withdrawal and preventive therapy.[1,7]
- Eptinezumab is an intravenously administered, high-affinity anti-CGRP (calcitonin gene-related peptide) monoclonal antibody approved for migraine prevention,[8] offering full bioavailability by the end of the infusion and rapid CGRP inhibition.
- The RESOLUTION trial assessed the efficacy and safety of eptinezumab *vs* placebo when given in addition to patient education in participants with CM and MOH.[9]
  - The trial met its primary and all key secondary endpoints.

Objective

- To evaluate the impact of eptinezumab *vs* placebo on patient-reported outcomes measuring headache-related burden, migraine-related disability, work productivity and activity impairment, health-related quality of life, and treatment satisfaction in adults with CM and MOH who also received a brief educational intervention (BEI).

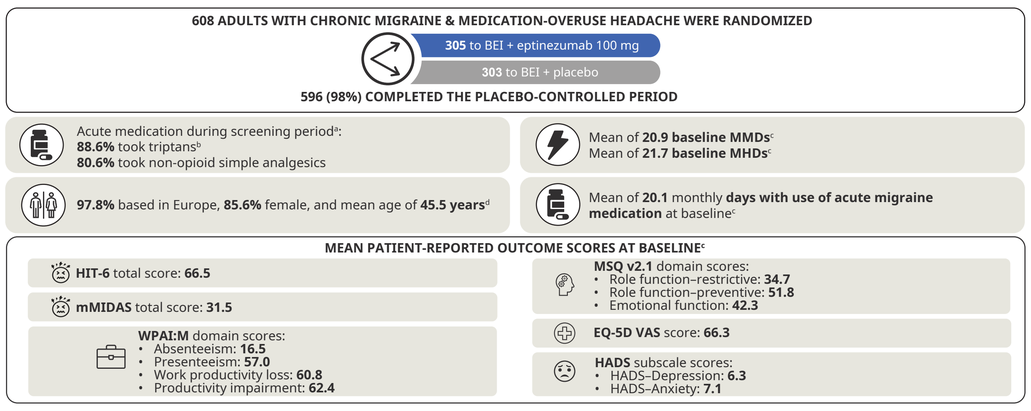
Methods

- RESOLUTION was a multinational, double-blind, randomized, placebo-controlled phase 4 trial (ClinicalTrials.gov: NCT05452239).[9]
- The trial comprised a 4-week screening period; 12-week, double-blind, placebo-controlled period; 12-week, open-label, extension period; and 8-week, safety follow-up period.
- Eligible adults (18–75 years) were diagnosed with CM and MOH (excluding opioid-overuse headache) and had ≥15 monthly headache days (MHDs), ≥8 monthly migraine days (MMDs), and regular overuse of acute medication (use on ≥10 or ≥15 days per month, depending on class of acute treatment[5]) during the 3 months prior to screening and during the screening period.
- At the end of the screening period, eligible participants entered the placebo-controlled period and were randomized (1:1) to infusion with eptinezumab 100 mg or placebo, with all participants receiving an ~10-minute standardized BEI about MOH (semi-structured educational conversation)[9,10] prior to the first infusion (i.e., at the baseline visit).
  - After the placebo-controlled period, all participants entered a 12-week open-label period in which they received eptinezumab 100 mg.
- Patient-reported outcome questionnaires were captured at prespecified time points using a self-reported electronic diary.
- Prespecified patient-reported outcome endpoints included:
  - **Patient Global Impression of Change (PGIC)** (quantifies overall impression of change in disease status; lower scores are better): score at Weeks 4 and 12
  - **6-item Headache Impact Test (HIT-6)** (quantifies headache-related life impact; lower scores are better): change from baseline to Weeks 4 and 12 in total score
  - **modified Migraine Disability Assessment (mMIDAS)** (quantifies migraine-related disability; lower scores are better): change from baseline to Weeks 4 and 12 in total score
  - **Migraine-specific Work Productivity and Activity Impairment questionnaire (WPAI:M)** (quantifies migraine-related impairment in workplace productivity and everyday activities; lower scores are better): change from baseline to Weeks 4 and 12 in each domain score
  - **Migraine-Specific Quality-of-Life questionnaire version 2.1 (MSQ v2.1)** (quantifies migraine-related quality of life; higher scores are better): change from baseline to Weeks 4 and 12 in each domain score
  - **EQ-5D-5L visual analogue scale (EQ-5D VAS)** (quantifies overall health-related quality of life; higher scores are better): change from baseline to Weeks 4 and 12 in score
  - **Hospital Anxiety and Depression Scale (HADS)** (quantifies the level of anxiety and depression; lower scores are better): change from baseline to Weeks 4 and 12 in each domain score
  - **9-item Treatment Satisfaction Questionnaire for Medicine (TSQM-9)** (quantifies patient satisfaction with the trial medication; higher scores are better): score at Weeks 4 and 12 in each domain
- Data were analyzed in the full analysis set (all randomized participants who received an infusion of eptinezumab or placebo in the placebo-controlled period, and who had a valid baseline assessment and at least one valid post-baseline 4-week assessment of MMDs across Weeks 1–12).
- All *p*-values comparing eptinezumab and placebo are descriptive and not adjusted for multiplicity.

Results

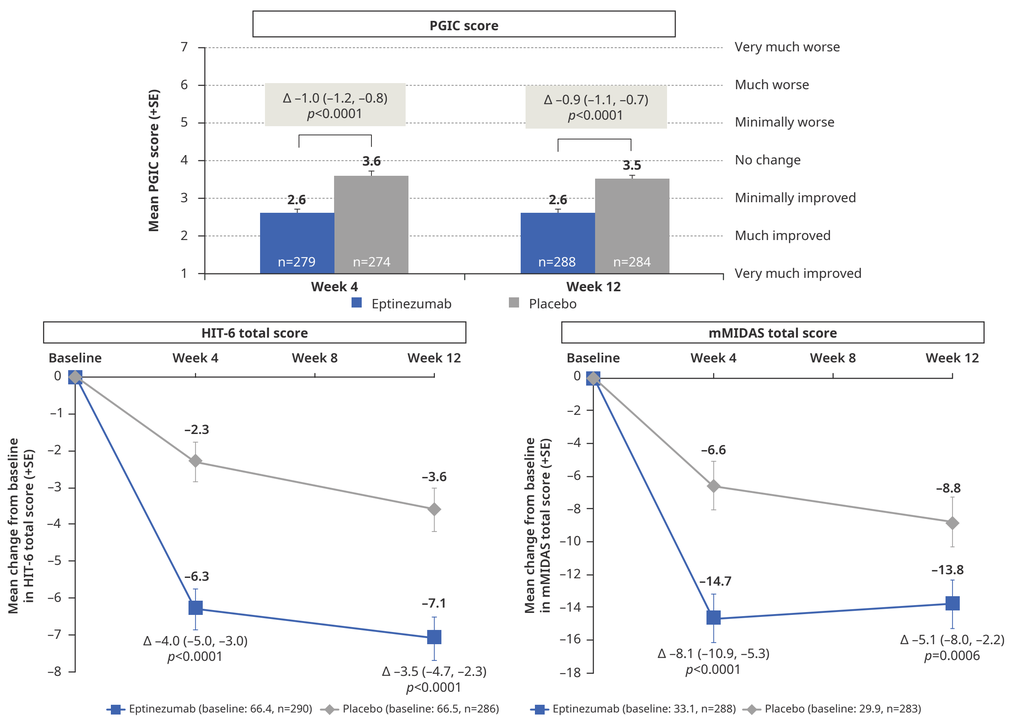
- Of 608 participants randomized, 596 (98.0%) completed the placebo-controlled period.
- Mean baseline scores (e.g., HIT-6 and mMIDAS total scores) were indicative of moderate to severe disease-related burden and poor health-related quality of life (**Figure 1**).
- Eptinezumab with BEI was associated with better (lower) PGIC scores than placebo with BEI at Week 4 ($p<0.0001$) and Week 12 ($p<0.0001$) (**Figure 2**).
- The eptinezumab arm was associated with greater improvements in HIT-6 total scores *vs* the placebo arm at Week 4 and Week 12 ($p<0.0001$, both comparisons) (**Figure 2**), with a clinically meaningful change from baseline in mean score with eptinezumab (i.e., >5-point improvement).[11,12]
- The mMIDAS total score improved more with the eptinezumab arm than with the placebo arm at Week 4 ($p<0.0001$), which was sustained at Week 12 ($p=0.0006$) (**Figure 2**), with a clinically meaningful change from baseline in mean score with eptinezumab (i.e., >30% improvement).[12]
- The eptinezumab arm was more favorable than the placebo arm for improving WPAI:M work productivity loss (**Figure 3**) and other WPAI:M sub-scores (**Table 1**) at Week 4 ($p<0.05$ *vs* the placebo arm for all comparisons), with benefits sustained at Week 12 ($p<0.01$ *vs* the placebo arm for all comparisons except absenteeism, which had low baseline scores).
- The observed increases in EQ-5D VAS score (**Figure 3**) and MSQ v2.1 domain scores (**Table 1**) at Weeks 4 and 12 showed that eptinezumab improved quality of life more than placebo ($p<0.01$ for all comparisons).
- The changes from baseline in HADS-Anxiety and HADS-Depression subscale scores were greater for the eptinezumab arm than for the placebo arm at Week 4 ($p<0.01$, both comparisons), with greater improvements sustained at Week 12 ($p<0.001$, both comparisons) (**Table 1**).
- TSQM-9 scores for effectiveness, convenience, and overall satisfaction were greater for the eptinezumab arm *vs* the placebo arm at Week 4 and sustained at Week 12 ($p<0.001$ for all comparisons) (**Table 1**).

Figure 1. Demographics and baseline characteristics



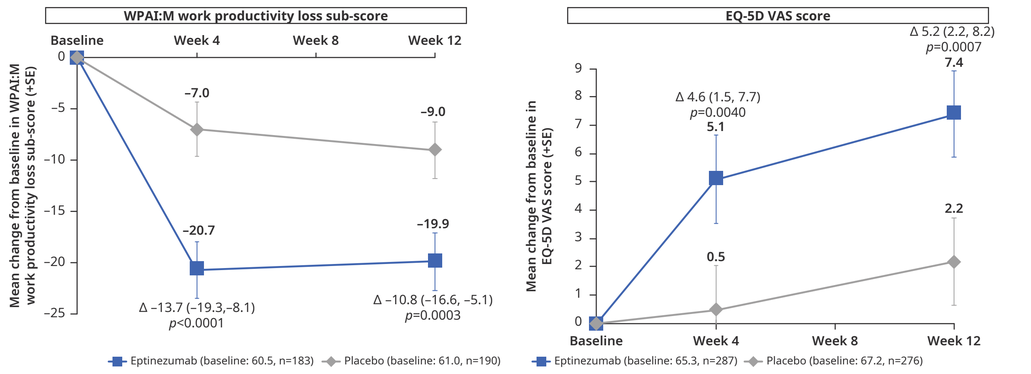
[a]Calculated using data from the electronic diary during the screening period and analyzed in the all-participants-treated set. [b]Includes triptan and/or ergotamine use; a total of 4 participants used ergotamine during the screening period. [c]Values are mean scores, calculated using data from the electronic diary during the screening period (in alignment with the baseline visit for patient-reported outcomes) and analyzed in the full analysis set. [d]Calculated using data collected at the first screening visit and analyzed in the all-participants-treated set. BEI, Brief Educational Intervention; HADS, Hospital Anxiety and Depression Scale; HIT-6, 6-item Headache Impact Test; MHDs, monthly headache days; MMDs, monthly migraine days; mMIDAS, modified Migraine Disability Assessment; MSQ v2.1, Migraine-Specific Quality of Life questionnaire, version 2.1; VAS, visual analogue scale; WPAI:M, Migraine-specific Work Productivity and Activity Impairment.

Figure 2. PGIC score and changes from baseline in HIT-6 total score and mMIDAS total score at Weeks 4 and 12



For all measures, lower scores are better. The least-squares mean difference from placebo (95% confidence interval) is reported based on a mixed model for repeated measures. **Δ**, least-squares mean difference from placebo; HIT-6, 6-item Headache Impact Test; mMIDAS, modified Migraine Disability Assessment; PGIC, Patient Global Impression of Change; SE, standard error.

Figure 3. Changes from baseline in WPAI:M work productivity loss sub-score and EQ-5D VAS score at Weeks 4 and 12



WPAI:M assesses activities related to workplace productivity loss over the preceding 7 days; lower scores are better. For EQ-5D VAS, higher scores are better. The least-squares mean difference from placebo (95% confidence interval) is reported based on a mixed model for repeated measures. **Δ**, least-squares mean difference from placebo; SE, standard error; VAS, visual analogue scale; WPAI:M, Migraine-specific Work Productivity and Activity Impairment.

Table 1. Changes from baseline in WPAI:M, MSQ, and HADS sub-scores, and TSQM-9 domain scores at Weeks 4 and 12

	Treatment arm	Change from baseline to Week 4	Difference from placebo at Week 4	Change from baseline to Week 12	Difference from placebo at Week 12
WPAI:M sub-score: Absenteeism[a]	**Eptinezumab,** n=195	**−4.7 (2.04)**	**−4.6 (−8.9, −0.4)** $p=0.0338$	**−4.7 (2.34)**	**−3.5 (−8.8, 1.7)** $p=0.1881$
	Placebo, n=196	**−0.1 (2.00)**		**−1.2 (2.32)**	
WPAI:M sub-score: Presenteeism[a]	**Eptinezumab,** n=183	**−20.3 (2.57)**	**−13.1 (−18.4, −7.8)** $p<0.0001$	**−19.1 (2.60)**	**−9.0 (−14.4, −3.6)** $p=0.0011$
	Placebo, n=190	**−7.2 (2.50)**		**−10.1 (2.54)**	
WPAI:M sub-score: Activity impairment[a]	**Eptinezumab,** n=287	**−20.7 (2.13)**	**−12.6 (−16.9, −8.3)** $p<0.0001$	**−18.9 (2.07)**	**−8.5 (−12.5, −4.4)** $p<0.0001$
	Placebo, n=276	**−8.2 (2.14)**		**−10.4 (2.08)**	
MSQ domain score: Role function-restrictive[b]	**Eptinezumab,** n=287	**24.0 (1.90)**	**13.9 (10.2, 17.6)** $p<0.0001$	**22.6 (1.87)**	**10.8 (7.2, 14.3)** $p<0.0001$
	Placebo, n=277	**10.2 (1.90)**		**11.8 (1.88)**	
MSQ domain score: Role function-preventive[b]	**Eptinezumab,** n=287	**18.6 (1.86)**	**10.7 (7.1, 14.3)** $p<0.0001$	**18.0 (1.83)**	**7.8 (4.3, 11.3)** $p<0.0001$
	Placebo, n=277	**7.9 (1.86)**		**10.2 (1.84)**	
MSQ domain score: Emotional function[b]	**Eptinezumab,** n=287	**23.8 (2.14)**	**13.7 (9.6, 17.8)** $p<0.0001$	**22.1 (2.19)**	**10.4 (6.1, 14.7)** $p<0.0001$
	Placebo, n=277	**10.1 (2.15)**		**11.7 (2.19)**	
HADS subscale score: Anxiety[a]	**Eptinezumab,** n=287	**−1.3 (0.26)**	**−0.8 (−1.4, −0.3)** $p=0.0017$	**−1.4 (0.26)**	**−1.0 (−1.5, −0.5)** $p<0.0001$
	Placebo, n=276	**−0.5 (0.26)**		**−0.4 (0.26)**	
HADS subscale score: Depression[a]	**Eptinezumab,** n=287	**−1.6 (0.29)**	**−1.0 (−1.5, −0.4)** $p=0.0006$	**−1.8 (0.30)**	**−1.2 (−1.8, −0.6)** $p<0.0001$
	Placebo, n=276	**−0.6 (0.30)**		**−0.6 (0.30)**	
		Week 4		Week 12	
TSQM-9 domain score: Effectiveness[b]	**Eptinezumab,** n=288	**58.2 (2.23)**	**19.2 (14.9, 23.5)** $p<0.0001$	**58.0 (2.26)**	**17.1 (12.6, 21.5)** $p<0.0001$
	Placebo, n=281	**39.0 (2.24)**		**40.9 (2.28)**	
TSQM-9 domain score: Convenience[b]	**Eptinezumab,** n=288	**69.6 (1.74)**	**6.0 (2.6, 9.3)** $p=0.0005$	**69.4 (1.79)**	**6.3 (2.8, 9.8)** $p=0.0005$
	Placebo, n=281	**63.6 (1.74)**		**63.1 (1.80)**	
TSQM-9 domain score: Overall satisfaction[b]	**Eptinezumab,** n=288	**59.6 (2.10)**	**16.0 (12.0, 20.0)** $p<0.0001$	**62.5 (2.14)**	**15.6 (11.4, 19.7)** $p<0.0001$
	Placebo, n=281	**43.6 (2.10)**		**47.0 (2.15)**	

The n-values represent the number of participants with available baseline data, except for TSQM-9, which uses Week 12 values because the measure was not captured at baseline. Scores and change from baseline values are LS mean (SE); difference from placebo values are LS mean (95% CI) based on a mixed model for repeated measures, with *p*-values vs the placebo arm provided. [a]Lower scores are better. [b]Higher scores are better. CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; LS, least-squares; SE, standard error; TSQM-9, 9-item Treatment Satisfaction Questionnaire for Medicine; WPAI:M, Migraine-specific Work Productivity and Activity Impairment questionnaire.

Key Points

- In the RESOLUTION trial, eptinezumab improved all patient-reported outcomes more than placebo in participants with CM and MOH who also received a brief educational intervention prior to dosing.
- At the first post-baseline time point (Week 4), greater improvements were observed for the eptinezumab arm than the placebo arm in patient-reported overall clinical impression of change, impact and burden of migraine, migraine-related work productivity and activity impairment, and health-related quality of life (migraine-specific and overall). Greater treatment satisfaction was also demonstrated in the eptinezumab arm compared to the placebo arm.
- The greater improvements in patient-reported outcomes and greater treatment satisfaction at Week 4 for the eptinezumab arm vs the placebo arm were sustained at Week 12.

Conclusion

- In people living with CM and MOH, following a brief educational intervention, eptinezumab was more effective than placebo in reducing migraine-related burden and impact, while improving work productivity and health-related quality of life.

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Declarations of conflicting interests

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